Hutchison China MediTech

Outlook

An emerging global biopharma

Hutchison China MediTech (HCM) has announced positive data that key late-stage asset surufatinib met the primary endpoint of PFS in non-pancreatic NET at the Phase III interim analysis. This translates to an earlier than expected China NDA submission (H219) and the potential launch of HCM's first un-partnered asset (early 2021). In China, partner Lilly has launched Elunate (fruquintinib) capsules. Early sales look promising and its potential inclusion on the China NRDL later this year will be definitive to the China opportunity. However, failure of fruquintinib monotherapy in third-line NSCLC and the changes in strategy to savolitinib in RCC has negatively affected our valuation. We forecast two further product launches on the horizon in 2021/2022 (China launch of fruquintinib in gastric cancer and global launch of savolitinib in NSCLC). CKH has completed a secondary offering of ADSs, which has reduced its holding to 51.15% (from 60.2% previously). We see this as a significant positive for HCM as it increases the free float, potentially leading to better liquidity. We value HCM at $5.6bn ($42.23/ADS) vs $6.5bn previously.

Year end	Revenue (US$m)	Net profit* (US$m)	EPADS ($)	DPADS ($)	P/E (x)	Gross yield (%)
12/17	241.2	(26.7)	(0.02)	0.0	N/A	N/A
12/18	214.1	(74.8)	(0.06)	0.0	N/A	N/A
12/19e	182.9	(141.2)	(0.11)	0.0	N/A	N/A
12/20e	194.4	(141.9)	(0.11)	0.0	N/A	N/A

Elunate launched, surufatinib to follow shortly

Elunate is now being commercialized in China (third-line CRC) by partner Eli Lilly (Lilly), a major inflection point for HCM and validation of its R&D philosophy. The positive interim readout of surufatinib (met primary endpoint of PFS) in the SANET-ep Phase III trial in non-pancreatic NET (trial was able to be stopped early) is of huge importance and these data will support a China NDA submission in late 2019. The years 2021/2022 are pivotal; partner AstraZeneca (AZN) could launch savolitinib in China for NSCLC (MET exon 14) and could become HCM's first asset to launch internationally (2022) in combination with Tagrisso for NSCLC.

Combination strategies to drive future growth

HCM has accelerated global (ex-China) development of its wholly owned assets (fruquintinib, surufatinib, HMPL-523 and HMPL-689). Ongoing advances and thus changes in treatment paradigms in many oncology indications mean that combination therapy is the best approach to treat resistant cancers. With this in mind, HCM has announced four new PD-1 collaborations for fruquintinib and surufatinib. HCM/AZN are focusing savolitinib's ex-China strategy on its use in combination with Tagrisso in MET-driven NSCLC, a blockbuster opportunity.

Valuation: $5.6bn ($42.23/ADS)

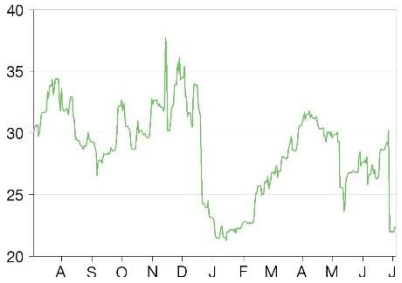
We value HCM at $5.6bn ($42.23/ADS) vs $6.5bn previously. Our revised valuation takes into account the success of the SANET-ep Phase III trial, failure of fruquintinib monotherapy in third-line NSCLC and the changes in strategy to savolitinib in RCC. We have additionally adjusted our product timelines to include combination strategies across the portfolio and revisited our R&D and S&M costs.

Pharma & biotech

5 July 2019

Price	**US$22.32**
Market cap	**US$2,975m**
	ADR/Ord conversion ratio 0.2
Net cash (US$m) as at 30 April 2019	236.2
ADRs in issue	133.3m
ADR Code	HCM
ADR exchange	NASDAQ
Underlying exchange	AIM
Depository	Deutsche Bank

ADR share price performance



52-week high/low	$37.7	$21.3

Business description

Hutchison China MediTech is an innovative China-based biopharmaceutical company targeting the global market for novel, highly selective oral oncology and immunology drugs. Its established commercial platform business continues to expand its outreach.

Next events

Surufatinib non-pancreatic NET Phase III (SANET-ep) data presentation	H219
Elunate (fruquintinib capsules) inclusion on China NRDL	H219
Surufatinib pancreatic NET Phase III interim data (SANET-p)	End-2019

Analysts

Dr Susie Jana	+44 (0)20 3077 5700
Dr Daniel Wilkinson	+44 (0)20 3077 5734
Dr Sean Conroy	+44 (0)20 3077 5700

healthcare@edisongroup.com

Edison profile page

Investment summary

Our long-term investment cases rests on HCM's ability to develop and commercialize its assets in both China and the rest of the world (RoW). HCM is rapidly investing in international expansion with five drug candidates in or about to enter global clinical trial development. Fruquintinib, savolitinib and surufatinib lead the pack with the earlier-stage spleen tyrosine kinase (Syk) and PI3K inhibitors coming to the fore. The launch of Elunate (fruquintinib) in China (November 2018) is a significant milestone for HCM, while the successful and early readout (June 2019) of surufatinib in the SANET-EP Phase III trial in non-pancreatic neuroendocrine tumors (NET) supports a China New Drug Application (NDA) submission in late 2019 and a potential launch early 2021. Key to HCM's global ambitions is SAVANNAH, the registrational study of savolitinib in combination with Tagrisso in non-small-cell lung cancer (NSCLC) patients. Clinical trials design and execution will become ever more critical in the fast-changing treatment landscape for oncology and we believe HCM remains committed to driving forward only assets and strategies that will have a material impact on returns. Combining its pipeline with approved and novel targets will be of great importance in the future of cancer treatment paradigms.

Recent market update: Increased free float

CK Hutchison Holdings Limited (CKH) has completed a secondary offering of ADSs, which has reduced its holding to 51.15% (from 60.2% previously). We see this as a significant positive for HCM as it increases the free float, potentially leading to better liquidity. We note this has had no effect on shares in issue and does not dilute any current shareholders. In connection with this offering, HCM, its officers and directors, in addition to CKH have agreed to a 90-day lock-up on sale or transfer of ordinary shares. As a result of this the proposed Hong Kong (SEHK) listing is now on hold. However, HCM has reiterated its commitment to the listing and a concurrent global offering of ordinary shares and may still pursue both following the cessation of the lock-up. An eventual listing on SEHK will be determined on a number of factors including, but not limited to, management decisions and market conditions. In our view, a capital raise on existing markets (AIM/NASDAQ) still remains likely in the next 12–24 months, however, cash resources as last reported (at 31 March 2019) of $391.2m are more than sufficient to enable current operational and strategic goals.

Valuation: $5.6bn ($42.23/ADS)

We value HCM at $5.6bn ($42.23/ADS) vs $6.5bn previously. We use a risk-adjusted net present value (NPV) method to discount future cash flows for the innovation platform (IP) (valuation of $4,004m). We have adjusted our valuation to reflect the success of the SANET-ep Phase III trial, the failure of fruquintinib monotherapy in third-line NSCLC (FALUCA), the cessation of enrolment in the SAVOIR (savolitinib monotherapy in the papillary renal cell carcinoma (PRCC)) study and the discontinuation of the clear cell RCC monotherapy trial (component of CALYPSO trial) in favor of combination strategies. Additionally, launch dates for key assets have been pushed back, while time to peak sales in China has been brought in line with our assumptions for the RoW and peak sales assumptions have been updated. We use earnings-based multiples for HCM's commercial platform (CP) (subs and JVs), applying a 20.4x multiple on our forecast 2019 net attributable profit (equity in earnings of equity investees, net of tax) for the JVs of $39.2m yields a valuation of $800.4m. We note that the significant increase in our terminal value from $3.70/ADS to $7.67/ADS is driven by the adjustment of time horizons, notably the terminal value now captures a greater proportion of key product sales. Adding April 2019 net cash and netting out unallocated costs results in a value of $5.6bn.

Sensitivities: Changing treatment landscapes

HCM is subject to the usual biotech and drug development risks, including clinical development delays or failures, regulatory risks, competitor successes, partnering setbacks, and financing and commercial risks. We note that the rapidly advancing oncology treatment landscape remains a key sensitivity with potential for clinical trial programs to become irrelevant while in progress (as evidenced by the cessation of the SAVIOR Phase III study) or for early efficacy readouts (eg surufatinib SANET-ep) to bring forward regulatory submissions and potential launch dates. In China, regulatory and reimbursement changes mean drugs have a potential faster route to approval and reimbursement than historically; China is becoming an increasingly important market for innovation drugs given supportive government policies and population size.

Financials: Funded to inflection points

Full-year 2018 results published in March 2019 highlighted robust growth in net profit attributable to the commercial platform division in China, coupled with clinical progress within the IP portfolio. HCM reported available cash resources of $391.2m (at 31 March 2019) at the group level (cash and cash equivalents including short-term investments of $271.9m, and unutilized bank borrowing facilities of $119.3m). In May 2019 HCM entered into a credit agreement with HSBC for an additional $51.3m unsecured credit facility. This, combined with the net profit generation from the CP division, means that HCM is well funded to key value inflection points (NDA submissions for savolitinib, surufatinib and fruquintinib in 2019–2021), even taking into account the considerable rise in R&D expenses seen in 2018, which we expect to continue to rise in the near term.

China: A stepping stone to global ambitions

With HCM's financial strength and its drive to retain the economic value of its assets, the next steps for the company are to commercialize its own assets in China then internationally (outside of current partnerships). The launch of Elunate (HCM's first internally developed asset) in China is a significant milestone for HCM and gives us confidence in the company's ability to execute on its R&D philosophy of building first- or best-in-class molecules with lower toxicity profiles to enable combination-based strategies for the treatment of cancers. We expect next approvals in China for surufatinib in NET, savolitinib in NSCLC (MET Exon 14 skipping) and fruquintinib in gastric cancer.

Outside China, HCM is now accelerating its operations as it transitions into a global biopharma; importantly, clinical and regulatory teams are now fully operational in the US and EU. HCM's first global approval (we forecast launch in 2022) in the US/EU could be for a savolitinib combination with AZN's Tagrisso in epidermal growth factor receptor mutant (EGFRm), MET+ NSCLC. Exhibit 1 highlights the numerous clinical milestones, both in China and globally, likely in 2019.

Exhibit 1: Potential key milestones for 2019

Product	Indication	Date	Next news
Global			
Savolitinib	Gastric cancer	H219	**Data:** Preliminary Phase II data (VIKTORY) for savolitinib monotherapy or in combination with Taxotere in second-line gastric cancer
	NSCLC	H219	Announce plans for further US Phase II/III studies in NSCLC
Fruquintinib	CRC	H219	Initiation of a US Phase II/III pivotal trial in 3/4L CRC
	Solid tumors	H219	Initiation of Phase I/Ib PD-1 combination trial
Surufatinib	Solid tumors	H219	Initiation of Phase I/Ib PD-1 combination trial
China			
Savolitinib	NSCLC	H219	first-line Met Exon 14 deletion registration study (Phase II) fully enrolled
Fruquintinib	NSCLC	H219	**Data:** present data from the FALUCA trial
Surufatinib	Pancreatic NET	End-2019	**Data:** Phase III interim data (SANET-p)
	Non-pancreatic NET	H219	**Data:** Presentation at conference of data set from the positive SANET-ep Phase III trial
HMPL-523	Indolent NHL	H219	Initiation of registrational study
	Idiopathic thrombocytopenic purpura (ITP)	H219	Initiation of Phase I trial

Source: HCM presentations, Edison Investment Research

China: Launch of Elunate marks the start of things to come

Eli Lilly launched Elunate (third-line colorectal cancer (CRC) patients) in November 2018 (at 31 March 2019 HCM reported $0.978m in royalties, implying $6.5m Elunate end-user sales in Q119) and the next development focus is on Phase III gastric cancer (FRUTIGA), for which approval could occur in 2021/22.

The recent successful efficacy read-out of surufatinib in the SANET-EP Phase III trial in non-pancreatic NET was earlier than we had anticipated and positions surufatinib as the next internally developed R&D asset to launch in China; HCM will hold a pre-NDA meeting with the China National Medical Products Administration to discuss the preparation of the NDA. Additionally, in China, registration studies continue for savolitinib in MET Exon 14 deleted NSCLC patients (primary data early-2020) and in surufatinib in pancreatic NET (interim data end-2019). Elunate and surufatinib mark the start of multiple potential drug launches in the near term.

Global: Infrastructure in place as clinical program expands

Our analysis concludes that much higher economic value resides in the strategy to develop and commercialize HCM's own assets, in particular with respect to fruquintinib (ex-China), surufatinib, epitinib, HMPL-523 and HMPL-689. HCM is now accelerating its global operations as it transitions into a global biopharma with clinical and regulatory (C&R) teams now fully operational in the US and EU. HCM plans to expand its US and EU C&R operations (headquartered in New Jersey, US) to 30 employees by end 2019 and further expansions should be expected in subsequent years as HCM builds ex China commercial infrastructure ahead of the potential launch of non-partnered assets surufatinib and fruquintinib (subject to positive clinical trial data and regulatory approval).

Global development is currently focused on savolitinib (with partner AZN) with multiple late-stage trials in progress, including SAVANNAH (second-line/third-line EGFRm, Tagrisso refractory, MET positive NSCLC with Tagrisso), CALYPSO (papillary and clear cell RCC with/without PD-L1 Imfinzi), and VIKTORY (MET-positive gastric cancer). Additionally, a proof-of-concept trial has initiated in Canada testing savolitinib in MET positive prostate cancer.

HCM's first approval (we forecast launch in 2022) in the US and EU could be for a savolitinib plus Tagrisso combination in MET+ NSCLC patients. AZN's Tagrisso has quickly become the standard of care in first-line NSCLC patients who have an EGFR mutation (EGFRm). Following Tagrisso treatment, the most common mutation is c-MET and AstraZeneca sees savolitinib as key to its strategy for MET driven NSCLC. In addition to savolitinib, HCM has already commenced the global development program for fruquintinib (CRC US registration study in planning based on China FRESCO data and completed US Phase I/II data) and surufatinib (US Phase I/II pancreatic NET

ongoing). Additionally, development programs for HMPL-523 (Syk inhibitor) and HMPL-689 (PI3Kδ inhibitor) in indolent NHL are expected to start Phase I/Ib trials shortly. We forecast global launches from 2022.

Worldwide: Combinations the focus across regions

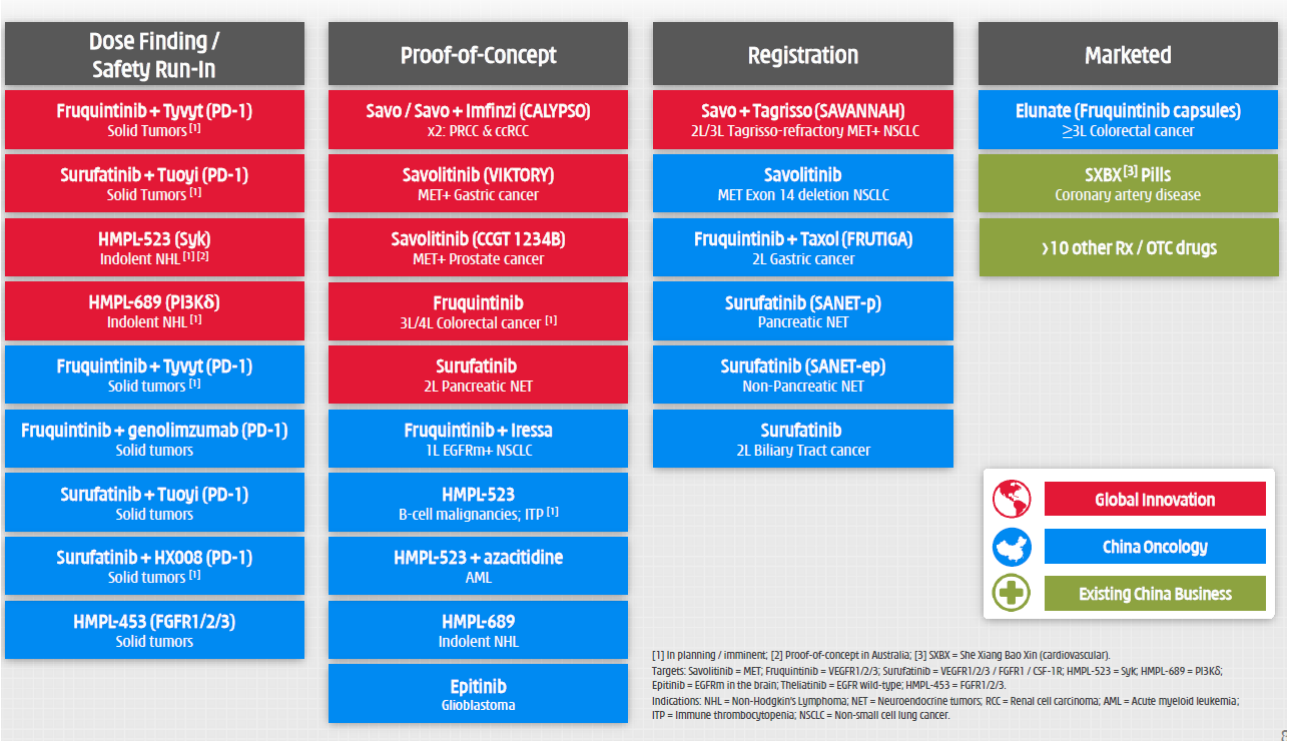
HCM's R&D efforts has successfully generated a portfolio of candidates that address existing, well-validated targets with lower toxicity profiles as a result of target selectivity. Cleaner toxicity profiles should enable drug combination as often lack of tolerability leads to failure. Combinations of targeted therapies (TKI (tyrosine kinase inhibitor), monoclonal antibodies and immunotherapies) and chemotherapy is increasingly becoming the best approach to treating the complex and constantly mutating disease that is cancer.

In the last 12 months HCM has signed four co-development collaborations for fruquintinib and surufatinib in combination with a variety of China developed PD-1 (programmed cell death protein-1) monoclonal antibodies. Advances in the field of immune oncology in the last few years and the increasing understanding that different classes of cancer drugs (targeted therapies and checkpoint inhibitors) may act synergistically together means that the industry needs to keep up the pace and ensure that trial design and combinations address the most pertinent question of all: which drug regimen is best for a given cancer. HCM's partnership with AstraZeneca means that savolitinib's international focus is on combinations with a number of AZN's oncology drugs including Tagrisso and Imfinzi. The renegotiated deal with Lilly for fruquintinib has given HCM freedom to explore different line extensions and combinations through non-restrictive collaborations.

Pipeline overview

HCM has multiple tyrosine kinase inhibitors in clinical development, with eight assets in the clinical phase of development across over 30 trials globally, including five registration studies that are expected to read out over the next 24 months. Exhibit 2 provides an overview of the pipeline and segments the asset opportunity by China NDA opportunities (blue) and the international drug development programs (red). Assets marketed through China CP are in green.

Exhibit 2: Portfolio summary



Source: Hutchinson China MediTech

In the next sections we discuss in turn:

- **Elunate/fruquintinib capsules:** launched with partner Lilly in China for mCRC in November 2018. FRUTIGA is another trial investigating combination with Taxol in gastric cancer; top-line data are expected in 2020. With FALUCA missing its primary endpoint in NSCLC, HCM will now explore PD-1 combinations that could drive earlier use.
- **Savolitinib**: two pivotal studies in NSCLC are ongoing – in China for MET Exon 14 skipping and globally for a Tagrisso savolitinib combination (SAVANNAH). The PRCC strategy will focus on a combination with a PD-L1 inhibitor following changes in renal cancer treatment paradigms.
- **Surufatinib**: China NDA filing in 2019 for non-pancreatic NET. This would be the first un-partnered launch of an HCM asset.
- **HMPL-523** and **HMPL-689**: a Phase I/Ib study in Australia and China has expanded its enrolment (blood cancers). IND applications for both HMPL-523 and HMPL-689 have been accepted for US and EU clinical development to start.

Elunate: Innovation into commercialisation

The launch of Elunate (fruquintinib capsules) for metastatic colorectal cancer (third-line and above) by partner Lilly in November 2018 was a defining moment for HCM, as the first of its IP assets to launch in China and the first China discovered and developed new drug for oncology to have full approval and reach the market. At 31 March 2019 HCM reported $0.978m in royalties, implying $6.5m Elunate sales in Q119. Elunate has been priced at $3,300 per monthly cycle (RMB21,960) and a patient-access program has been implemented to widen availability in China (patients pay for the first, second and fifth cycle). HCM's target patient population for third-line CRC is ~55,000–60,000 patients (third line is 15% of incidence in China of 380,000 patients per year). Importantly, inclusion on China's National Reimbursement Drug List (NRDL) will define the opportunity given full-scale reimbursement nationally. Inclusion on the list is conceivable in H219 as the Chinese

government agencies are reviewing inclusions and exclusions on the list much more frequently than in the past.

Exhibit 3 highlights the status of Fruquintinib clinical trials in China and internationally in a broad range of oncology indications.

Exhibit 3: Fruquintinib clinical trials

Treatment	Indication	Sites	Trial	Notes
Fruquintinib MT	third-line CRC (chemotherapy refractory)	China	Phase III FRESCO	Approved and launched
Fruquintinib MT	third-line/4L CRC (Stivarga/Lonsurf refractory/intolerant)	US/EU	Phase Ib	US/EU registration study in planning
Fruquintinib and Taxol	second-line gastric cancer	China	Phase III FRUTIGA	Top-line data 2020
Fruquintinib MT	third-line NSCLC (chemotherapy refractory)	China	Phase III FALUCA	Did not meet median OS (primary endpoint)
Fruquintinib and Iressa	NSCLC first-line (EGFRm+)	China	Phase II NCT02976116	Completed enrolment. Preliminary data presented at WCLC 2017.
Fruquintinib and genolimzumab (PD-1)	Solid tumors	China	Phase I	Ongoing
Fruquintinib and Tyvyt (PD-1)	Solid tumors	China	Phase I	Ongoing

Source: Edison Investment Research, Hutchison China MediTech. Note: MT: monotherapy.

Positive renegotiated Eli Lilly deal terms

In December 2018, HCM and Eli Lilly renegotiated their 2013 agreement on Elunate. Under the terms of the new deal (Exhibit 4), HCM has acquired the rights to determine for which indications (LCI: life cycle indications) it will further develop Elunate. HCM will now pay the full development costs of any future clinical development in China and in return will benefit from higher economic value retention including both higher approval milestones and royalties. HCM additionally now has the option to co-promote Elunate in China. On the occurrence of non-fruquintinib related Eli Lilly commercial action (which we assume is related to a China launch of Cyramza), HCM will be able to promote Elunate in provinces that represent 30–40% of sales of Elunate. Lilly will pay HCM a service fee for all promotional activities in the HCM regions. While HCM already has a significant salesforce in China, the co-promotion deal enables HCM to gain experience in commercializing its own in-house developed products and expand its oncology salesforce prior to launching other pipeline assets. Importantly, HCM retains the full development and commercial rights to fruquintinib outside of China (assuming regulatory approvals are achieved).

Exhibit 4: Eli Lilly amended deal terms

Terms	Original 2013 agreement	Amended 2018 agreement
LCI development costs – paid by Lilly	70%	0%
LCI development costs – paid by HCM	30%	100%
LCI regulatory approval milestones– paid to HCM	$12.5m	$20.0m (for up to 3 approvals)
Royalties – paid to HCM	15–20%	15–2 9%
Co-promotion rights in China (% of provinces)	0%	30–4 0%
Co-promotion service fees - paid to HCM (% of net sales)	0%	Not disclosed

Source: Hutchison China Meditech, Edison Investment Research. Note: LCI: Life cycle indications.

The renegotiated deal terms on Elunate (fruquintinib) are a major positive in our view as these give HCM freedom of control on development of the asset into multiple oncology indications, not just as a monotherapy but also in combination therapies, the newly announced collaborations with Innovent Biologics and Genor Biopharma signal this. With the simplification of the LCI decision-making process from two parties to one, we expect HCM will accelerate Elunate's commercial development in China beyond the indications currently in development, particularly in immunotherapy combinations.

FRUTIGA top-line data in gastric cancer expected in 2020

The National Central Cancer Registry of China reports an incidence of 679,000 gastric cancer cases and 498,000 gastric cancer deaths in China in 2015. Most Chinese gastric cancer patients receive chemotherapy and few targeted therapies are approved, with limited salvage treatments in third line and above. HCM has initiated a pivotal Phase III (FRUTIGA) combination trial (second line) evaluating fruquintinib and established chemotherapy agent Taxol (paclitaxel) for the treatment of advanced gastric cancer patients (n>500) who have progressed after first-line standard chemotherapy (5-fluorouracil and platinum doublets). If the FRUTIGA Taxol combination data are positive, this would enable fruquintinib use in earlier lines of gastric cancer. The full top-line data are expected in 2020. The primary efficacy endpoint for FRUTIGA was overall survival (OS); secondary endpoints included PFS (progression-free survival), ORR and DCR.

FALUCA primary OS endpoint not met in NSCLC

In November, HCM announced data from FALUCA, HCM's China-based Phase III trial for fruquintinib monotherapy in third-line NSCLC (after failure on two lines of systemic chemotherapy). The trial missed its primary endpoint of improving overall survival compared to placebo. The full dataset is yet to be presented (has been submitted for publication at a scientific conference), but statistically significant improvements were observed across all secondary endpoints (data not disclosed): PFS, duration of response (DoR) and objective response rate. Without a fully analyzed dataset, and ascertaining the underlying cause for missing this endpoint, the future direction for fruquintinib monotherapy in third-line NSCLC is unclear. What is becoming clear is that advances in cancer therapy, including targeted therapies and in the more nascent field of immunoncology, are changing treatment paradigms and this has implications for ongoing clinical trials that were designed and initiated a few years back (including FALUCA). Higher than expected survival rates seen in placebo arms could be a function of patients receiving other therapies at higher lines not accounted for when FALUCA was initially designed skewing the results. Thus we now assume that any future development in NSCLC is focused on combination therapies, particularly immunotherapy combinations (see below). While there are no planned combinations of fruquintinib with Tagrisso and/or savolitinib in NSCLC, we believe any combinations could be synergistic and provide a point of differentiation for fruquintinib.

PD-1 combination the focus for future development

Targeted therapies and immunotherapies (monotherapy) have improved patient outcomes across many tumor types; combinations that work synergistically could enhance results further. HCM has developed Elunate to compete in the ~$16bn vascular endothelial growth factor receptor (VEGFR) market, which is dominated by Roche's Avastin (bevacizumab), a VEGF-A inhibitor that is an intravenously administered monoclonal antibody (Roche reported 2018 sales of $6.9bn). Avastin inhibits VEGF A protein, whereas fruquintinib targets VEGF receptors.

In December 2018 the US FDA approved the triple combination of Tecentriq, Avastin and chemotherapy (carboplatin and paclitaxel) for first-line NSCLC (non-squamous), which is not driven by EGFR or ALK mutations (Exhibit 5). This serves as a strong validation that a combination of an anti-angiogenic agent (Avastin) with an immune checkpoint inhibitor (Tecentriq) can have added benefit to patients with NSCLC; this highlights the potential for fruquintinib and surufatinib (which both inhibit VEGFR1/2/3) in combination with PD-1 antibodies. Similarly, data from three pivotal studies investigating analogous combination therapies for RCC (IMmotion151, JAVELIN renal 101 and KEYNOTE426) look promising (Exhibit 5) and support combination use.

In November, HCM entered into a range of collaborations to test surufatinib and fruquintinib with PD-1 inhibitors. For fruquintinib, HCM has a global partnership with Innovent Biologics and its PD-1

inhibitor sintilimab (IBI308) and a China-focused collaboration with Genor BioPharma and its PD-1 inhibitor genolimzumab (GB226).

Exhibit 5: VEGF(R)/PD-(L)1 targeting combinations pivotal study data

Sponsor	Anti-angiogenic agent	Immune checkpoint inhibitor	Chemo-agent(s)	Trial/indication	Status
Roche	Avastin (bevacizumab) **VEGFA antibody**	Tecentriq (atezolizumab) **PD-L1 antibody**	Carboplatin & paclitaxel	IMpower150 **first-line NSCLC****	Combination received US FDA approval in December 2018 based on top-line data from the Phase III study, which demonstrated the triple combination of Avastin, Tecentriq and chemotherapy improved median OS relative to the control arm (Avastin and chemotherapy) irrespective of PD-L1 expression (19.2 vs 14.7 months) (HR 0.78; 95% CI, 0.64 to 0.96; p = 0.02).
			-	IMmotion151 **first-line ccRCC**	Data presented at ASCO 2018 showed combination improved median PFS compared to sunitinib monotherapy (11.2 vs 7.7 months) (HR 0.74; 95% CI, 0.57–0.96; p = 0.02) in PD-L1 +ve patients (> 1% tumor expression), which constituted 40% ITT population; mPFS across the intent to treat (ITT) population was also observed (11.2 vs 8.4 months) (HR 0.83; 95% CI, 0.70–0 .97; p = 0.02) – study ongoing to determine co-primary endpoint of OS.
Pfizer	Inlyta (axitinib) **VEGFR1/2/3 TKI***	Bavencio (avelumab) **PD-L1 antibody**	-	JAVELIN renal 101 **first-line ccRCC**	Data presented at ESMO 2018 showed a significant improvement in mPFS for the combination arm compared to the control arm on sunitinib monotherapy (13.8 vs 8.4 months) (HR 0.69, p < 0.0001) and ORR (51.4% vs. 25.7%; p <0.0001) irrespective of PD-L1 expression – trial is ongoing to determine co-primary endpoint of OS, but in February 2019 the US FDA granted priority review for an supplemental biologics licence application (sBLA) based on these interim data, setting a target action date of June 2019.
Merck	Inlyta (axitinib) **VEGFR1/2/3 TKI***	Keytruda (pembrolizumab) **PD-1 antibody**	-	KEYNOTE-426 **first-line ccRCC**	Data presented at ASCO GU 2019 showed a significant improvement in both mPFS for the combination arm compared to the control arm on sunitinib monotherapy (15.1 vs 11.1 months; HR 0.69, p < 0.0001) and ORR (59.3% vs 35.7%; p < 0.0001) irrespective of PD-L1 expression – in February 2019 the US FDA granted priority review for an sBLA based on these interim data, setting a target action date of 20 June 2019.

Source: ClinicalTrials.gov; table adapted/updated from that reported by Ramjiawan et al. Note: NSCLC – non small cell lung cancer; ccRCC – clear cell renal cell carcinoma; OC – ovarian cancer. *Also active against PDGFRα/β &c-Kit. **Non-squamous, stage IV.

Fruquintinib (Elunate) peak sales assumptions

We have revisited our fruquintinib (Elunate) expectations, in the light of the differing pricing strategy to our expectations, and the disappointing FALUCA data in NSCLC monotherapy and move to combination strategy in this indication. We forecast global peak sales for fruquintinib of $2.6bn across all indications under investigation (CRC, NSCLC and gastric cancer). The magnitude of fruquintinib's success in part will depend on the global opportunity; we forecast RoW launches from 2023. In China Elunate gross pricing is $3,300/month, but as a result of HCM's Patient Access Program, the median cost for Elunate over an average five months of use is $1,980/month. We now forecast peak sales of $199m in China vs $149m previously. We believe this pricing strategy and patient access program could increase hospital formulary access and we assume that Elunate will be added to China's NRDL in the near term, inclusion will be a major growth driver.

Exhibit 6: Fruquintinib peak sales forecasts

Product	Indication	Launch year/ peak sales China	Launch year/ peak sales RoW	2019 assumptions
Fruquintinib	CRC	2018/2022 $199m	2023/2027 $565m	Global new cases (1,500,000), China new cases (306,000). China penetration 6.0%, $3,300 per month, three months reimbursement as per patient access program. RoW penetration 0.7%, $5,000 per month, 12-month treatment duration.
	NSCLC	2025/2029 $393m	2025/2029 $721m	Global new cases (1,690,000), China new cases (623,000), China penetration 1.5%, $3,300 per month, 12-month treatment duration. RoW penetration 1.0%, $5,000 per month, 12-month treatment duration.
	Gastric cancer	2021/2025 $340m	2025/2029 $392m	Global new cases (1,034,000), China new cases (454,000). China penetration 2%, $3,300 per month, 12-month treatment duration. RoW penetration 1%, $5,000 per month, 12-month treatment duration.
	Deal economics			Deal economics: recently amended deal terms with an improved royalty rate of 15–29% in China, with HCM now funding majority of development costs but will receive $20m for every new indication in which Fruquintinib is approved (up to 3) in China. HCM retains all other global rights (ex-China) and will fund development and commercial costs worldwide.

Source: Edison Investment Research. We forecast peak sales in China as seven to eight years from launch, and five years from launch for RoW.

Savolitinib: Striving for combination success

Since our last report was published, much clinical progress in the field of MET-driven cancers has occurred. Foremost is changes in the renal cancer treatment paradigm. We had previously anticipated that savolitinib monotherapy for PRCC would be the first launched indication, potentially in late 2019 through a breakthrough approval in the US. However, recent paradigm shifts in the treatment of renal cell carcinomas are moving towards combinations with a PD-1 inhibitor. As such, AZN has suspended the Phase III monotherapy study in PRCC (SAVOIR) and future development will likely focus on a combination with AZN's PD-L1 inhibitor Imfinzi (see below); this decision also took into account data from the MES (molecular epidemiology study) which showed smaller than expected applicable MET+ status.

In the field of lung cancer, AZN's Tagrisso is raising the bar as it moves into the first-line setting in EGFR mutation-positive NSCLC, reporting sales of $1.9bn in 2018, its second full year on the market. The implication here is savolitinib's largest opportunity could be in combination with Tagrisso in EGFRm MET+ NSCLC patients as MET mutations are the biggest driver in Tagrisso resistance. The savolitinib/Tagrisso combination could rewrite the second-line/third-line treatment paradigm and our forecast peak sales could be conservative. Following the encouraging data seen from the TATTON study, AZN and HCM in December 2018 initiated the global registrational study SAVANNAH for Tagrisso refractory NSCLC patients. HCM's partnership with AZN remains crucial to the development of savolitinib and our forecast peak sales.

Savolitinib is a highly selective inhibitor of the c-Met signaling pathway and targets patients with resistant cancers whose tumor type tests positive for MET mutation, amplification or over expression. Savolitinib is hypothesized to have a greater beneficial impact on c-Met-driven tumors than approved multi-kinase inhibitors, particularly in EGFR-resistant patient subgroups. C-Met (or hepatocyte growth factor receptor/HGFR) is a signaling pathway, dysregulation of which mediates proliferation, apoptosis and migration in many tumor types including NSCLC, RCC and gastric cancer. This aberrant functioning can arise through c-Met gene amplification, c-Met over expression and gene mutations and the extent of each will differ by tumor type and patient. A key challenge in the area is identifying which biomarker and thus which diagnostic is most relevant to select the appropriate patients for MET targeted treatment as monotherapy and as combinations. Exhibit 7 highlights the incidence of MET dysregulation in NSCLC; the type (eg gene over expression, HGF expression, gene amplification, gene mutation) and the relevant biomarker for testing.

Exhibit 7: Type of MET aberration and relevant biomarkers

MET aberration	Function consequence	Biomarker
Gene over expression	Reduces or removes the requirement for ligand activation, leading to sustained or altered signaling properties of the kinase	MET/p-MET expression by IHC
Gene mutation	MET mutation can lead to reduced degradation, with consequent over expression and sustained or altered signaling	MET exon 14 skipping
Gene amplification	Can lead to over expression and reduce or remove the requirement for ligand activation, leading to sustained or altered signaling	MET GCN MET/CEP7 ratio
Gene rearrangement	May reduce or remove the requirement for ligand activation, leading to sustained or altered signaling	MET rearrangement
HGF expression	Ligand-induced activation could cause sustained or altered signaling	Circulating plasma HGF
Downstream MET signaling alteration	May reduce or remove the requirement for ligand activation, leading to sustained or altered signaling	CBL mutation

Source: Adapted from Molecular Cancer Therapeutics (2017) 555. Note: IHC = Immunohistochemistry.

We highlight that the field is still in many ways in its infancy as companies such as HCM and Novartis (capmatinib) are at the forefront of developing c-MET inhibitors. In late 2016 Phase III trial results of onartuzumab plus erlotinib in NSCLC did not prove clinical benefit over the comparator arm and it is thought that the clinical eligibility of patients based on MET over expression as

measured by IHC may not be sufficiently sensitive and specific as a diagnostic tool to identify MET positivity.

Exhibit 8: Savolitinib clinical development

Treatment	Indication	Sites	Trial	Notes
Savolitinib +Tagrisso	NSCLC (2/third-line EGFRm (TKI refractory; MET+)	Global	Phase Ib/II TATTON	Completed, interim data presented at AACR2019.
Savolitinib +Tagrisso	NSCLC (2/third-line EGFRm (Tagrisso refractory; MET+)	Global	Phase II SAVANNAH	Initiated December 2018
Savolitinib MT	NSCLC (first-line MET Exon 14 skipping)	China	Phase II NCT02897479	Enrolment completion expected end-2019
Savolitinib MT	Papillary RCC (MET+)	Global	Phase III SAVOIR	Suspended due to MES study and CALYPSO study
Savolitinib +Imfinzi	Papillary RCC	UK/Spain	Phase II CALYPSO	Interim data presented at ASCO GU 2019, primary completion expected
Savolitinib MT	Clear cell RCC (VEGFR TKI refractory)	UK/Spain	Phase II CALYPSO	Enrolment suspended, focus on the Imfinzi combination arm
Savolitinib +Imfinzi	Clear cell RCC (VEGFR TKI refractory)	UK/Spain	Phase II CALYPSO	Investigator sponsored study, data expected end-2019/early-2020
Savolitinib MT	Gastric cancer (MET amplification)	China	Phase II NCT01985555	Completed, data expected to be published H219
Savolitinib MT	Gastric cancer (MET amplification)	South Korea	Phase II VIKTORY	Completed, data expected to be published H219
Savolitinib +Taxotere	Gastric cancer (MET amplification)	South Korea	Phase II VIKTORY	Enrolment suspended due to high efficacy on the monotherapy arm
Savolitinib +Taxotere	Gastric cancer (MET over-expression)	South Korea	Phase II VIKTORY	Enrolment suspended due to high efficacy on the monotherapy arm
Savolitinib MT	Metastatic castration-resistant prostate cancer (mCRPC)	Canada	Phase II CCGT 1234B	Investigator sponsored study, primary completion end-2019

Source: Edison Investment Research, Hutchison China MediTech. Note: MT = monotherapy.

Tagrisso combination could rewrite NSCLC paradigm

In the NSCLC setting savolitinib is being evaluated as a monotherapy in the MET Exon 14 skipping China Phase III registration study, in combination with Tagrisso (global TATTON and SAVANNAH studies). We highlight the largest opportunity is increasingly becoming the Tagrisso plus savolitinib combination in resistant driven EGFRm+ MET + patient populations. In our view savolitinib's first approval for NSCLC ex China will likely be in combination with Tagrisso (AZN) for MET+, T790M± patients who have progressed following Tagrisso. This specific subset of patients has an unmet medical need and, although we forecast a 2022 launch, BTD award could lead to earlier approval and launch.

AZN has presented analyses of FLAURA (first-line Tagrisso) and AURA3 (second-line Tagrisso) data examining mutation status (via plasma sampling) of patients who become resistant to Tagrisso. While no known mechanism of resistance was identified in 60% of patients in AURA3, MET amplification was identified as an acquired resistance mechanism in 19% of patients and 15% of patients in FLAURA. Understanding the mechanism of acquired resistance following Tagrisso therapy is a key clinical question to inform the next treatment choice. AURA3 suggests that patients could benefit from addition of savolitinib to Tagrisso in MET +ve patients as second-line therapy.

Critical for the future clinical trials planned for savolitinib is understanding the width and breath of MET alteration and how it can be best detected (tissue biopsy vs plasma testing). More recently it has been recognized that MET amplification in NSCLC is implicated in acquired resistance to EGFR inhibitors in ~20% of cases with EGFR inhibitor resistance. A 2018 analysis of plasma samples from Tagrisso's AURA3 trial identified MET implication to be the cause of Tagrisso resistance in 19% of these patients in second-line and above. Data from the Tagrisso FLAURA trial suggest that MET amplification is implied in 15% of cases in first-line. In both cases, plasma samples were measured and it is thought that the frequency of MET amplification could be higher in tissue samples. This provides further therapeutic rationale for combinations of MET inhibitors with

EGFR inhibitors to resistant NSCLC and the question is how high up in the paradigm savolitinib can be used (in combination with Tagrisso). The SAVANNAH and ORCHARD (see below) studies that are underway should shed light on these questions.

TATTON data: Consistent with interim analysis

In 2014 AZN initiated the TATTON study, a multi-arm Phase Ib/II study to test the suitability of an array of therapies with Tagrisso (osimertinib) in EGFRm+ NSCLC patients who have progressed following treatment with EGFR TKIs. Patients who had cancer progression driven by MET amplification (identified by either NGS [next generation sequencing], FISH [fluorescence in situ hybridization] or IHC) were placed on a combination regime of savolitinib and osimertinib, stratified into two cohorts based on whether they had progressive disease (PD) while on a first- or second-generation EGFR TKI (ie Iressa/Tarceva) or a third-generation EGFR TKI (ie osimertinib). Data from these two dose-expansion cohorts were presented at AACR2019 (Cohort 1 and Cohort 2), and reaffirmed the tolerable safety profile and promising efficacy data from the preliminary analysis that was presented at WCLC2017.

Following the encouraging data seen from these arms of the TATTON study, AZN and HCM in December 2018 initiated the global registrational study SAVANNAH, a Phase II, single-arm trial assessing the efficacy of Tagrisso in combination with savolitinib for patients with EGFRm, MET-amplified, locally-advanced or metastatic NSCLC who have progressed, following treatment with Tagrisso. Primary data is expected in 2021. Likewise, AZN is planning to conduct ORCHARD, a Phase II, multiple-arm trial looking to identify the drivers of resistance in NSCLC patients who have progressed following first-line treatment with Tagrisso; this should act as a feeder to SAVANNAH and aid in patient recruitment.

NSCLC first China NDA submission in 2021

An estimated 2–3% of newly diagnosed NSCLC patients have a specific mutation known as MET Exon 14 skipping (Exon 14 of the MET gene is not functioning or deleted) leading to c-MET over expression. In China, HCM estimates this to be 10,000 patients. A registrational Phase II clinical trial is underway in such patients who have progressed on prior chemotherapy, or who are unable to tolerate additional rounds of chemotherapy. Although the patient size is relatively small, this indication could be savolitinib's first NDA in China. Interim data were presented at AACR2019 and of the 31 evaluable patients, 17 had a confirmed partial response (ORR of 54.8%), 12 patients had stable disease and two patients showed disease progression (DCR of 93.5%). Savolitinib was generally well tolerated, with only 14.5% (six of 41 patients) discontinuing treatment due to treatment emergent adverse events, mainly drug-induced liver toxicity (three patients); six patients died on treatment, one of which was suspected to be treatment related (tumor lysis syndrome). Trial recruitment (in China) is expected to complete in 2019 and completion/primary data can be expected in 2020, potentially with a Chinese NDA submission in 2021. We forecast launch in this indication in 2022. In the longer term in China, we believe a savolitinib plus Tagrisso combination will expand use in other subsets of NSCLC.

Data presented at ASCO2019 have highlighted the competitive landscape emerging (globally) for targeted treatments of MET Exon 14 skipping NSCLC patient populations; both Merck's c-Met inhibitor tepotinib and Novartis's capmatinib demonstrated impressive ORR when used in treatment naïve patients (59% and 68% respectively) and as 2/third-line treatments (45% and 41% respectively).

Kidney cancer: ICI combinations are game changing

The savolitinib registration strategy for kidney cancers, in particular PRCC, is being reassessed, taking into account findings from the molecular epidemiology study (MES) in PRCC patients and

the realization that treatment paradigms for RCC have shifted with the approval of PD-(L)1 inhibitors and increasing use of VEGFR inhibitors. As a result AZN and HCM have stopped enrolment of patients into SAVOIR, a Phase III global registration study evaluating savolitinib monotherapy (vs sunitinib monotherapy) in MET-driven PRCC patients. Successful commercialization of savolitinib in kidney cancer (both ccRCC and PRCC) now hinges on CALYPSO, an investigator sponsored Phase II study combining savolitinib with AstraZeneca's PD-L1 inhibitor Imfinzi (durvalumab).

In clear cell renal cell carcinoma (ccRCC) PD-(L)1 immune checkpoint inhibitor are revolutionizing the treatment landscape ; the combination of MET inhibition with PD-(L)1 inhibition could have utility in this space, as underlined by promising preliminary data from CALYPSO presently at ASCO GU 2019.

Savolitinib: Combined peak sales potential of $4.3bn

We forecast global peak sales for savolitinib of $4.3bn (PRCC, ccRCC, NSCLC and gastric cancer indications), lowered from our previous $5.9bn expectation. We have re-evaluated our assumptions following changes in market dynamics, and changes in cancer treatment paradigms. In our view savolitinib's first RoW approval for NSCLC will likely be in combination with Tagrisso (AZN) for MET+, T790M± patients. Additionally, we have reassessed our expected launch dates (and thus peak year of sales) and have pushed back launch years across indications (Exhibit 9), notably with the first indication launch (in second-line/third-line NSCLC) now forecast for 2022.

Exhibit 9: Savolitinib peak sales forecasts

Product	Indication	Launch year/ peak sales China	Launch year/ peak sales RoW	2019 assumptions
Savolitinib	PRCC	2024/2028 $64m	2022/2026 $267m	Global new cases (52,356), China new cases (8,443). China penetration 10.0%, $5,000 per month, 12-month treatment duration. RoW penetration 4.5%, $10,000 per month, 12-month treatment duration.
	ccRCC	2025/2029 $169m	2023/2027 $658m	Global new cases (141,611), China new cases (58,451). China penetration 4.0%, $5,000 per month, 12-month treatment duration. RoW penetration 2.0%, $10,000 per month, 12-month treatment duration.
	NSCLC	2022/2026 $387m	2022/2026 $1690m	Global new cases (1,829,310), China new cases (674,355). China penetration 0.8%, $5,000 per month, 12-month treatment duration. RoW penetration 1.0%, $10,000 per month, 12-month treatment duration.
	Gastric cancer	2023/2030 $326m	2024/2028 $757m	Global new cases (1,119,230), China new cases (491,420). China penetration 1.0%, $5,000 per month, 12-month treatment duration. RoW penetration 0.8%, $10,000 per month, 12-month treatment duration.
	Deal economics			$20m upfront fee (received in December 2011); $120m in development & regulatory milestones ($25m received as of December 2018) with hundreds of millions in commercial milestones (not disclosed); 30% royalty rate in China and 14–1 8% royalty rate ex-China (subject to approval for PRCC and providing aggregate sales remain below $5bn); AZN cover100% RoW development costs (excl $50m covered by HCM) and 75% of China development costs.

Source: Edison Investment Research. Note: We forecast peak sales in China as seven to eight years from launch, and five years from launch for RoW.

Surufatinib: Positive Phase III data, China NDA H219

Surufatinib (previously known as sulfatinib) could be the first of HCM's non-partnered assets to reach the China market in early 2021. The strategy for surufatinib was recently validated as positive interim data were announced in the SANET-ep Phase III trial testing surufatinib in non-pancreatic NET China patients. This was based on the trial meeting its primary endpoint of progression-free survival. The data support a China NDA submission in late 2019 and we forecast a launch in 2021. However, a launch could occur in late 2020. It previously took 15 months from submission of the NDA to approval for fruquintinib (Elunate). However, three months was to gain GMP certification for HCM's Suzhou manufacturing plant, which should not be necessary for surufatinib. If the NDA is submitted within four months (October 2019) of the recent announcement of the top-line data (as

was the case for fruquintinib), then we believe a launch in late 2020 is possible. However, predicting review timelines for the China FDA is notoriously difficult and this timeline could slip. As such, we currently retain our 2021 launch date. Additionally, a pivotal China Phase III study (SANET-p) in pancreatic NET is ongoing with data expected by the year end. If positive, this could further widen the market potential of surufatinib.

NETs are cancers that arise out of cells of the endocrine and nervous systems, predominately the digestive and respiratory tracts. While the current prevalence of NET in the US is ~150,000 patients (incidence of ~19,000 new cases per year), current treatment modalities are limited to subsets of NET with no broadly effective drugs across the NET spectrum. Data from Frost & Sullivan indicate the global NET market in 2018 was worth approximately $5.8bn and is expected to grow to $21.2bn by 2030. In particular, in China there is significant market opportunity with reported incidence of NET in 2018 of approximately 67,600.

Surufatinib is an oral angio-immunokinase inhibitor that targets VEGF1, 2 and 3; FGFR1 and colony stimulating factor 1 receptor (CSF-1R) kinases. CSF-1R is a cell-surface protein that acts as the receptor for the cytokine CSF1, which controls macrophage (a type of white blood cell) function. Inhibition of CSF-1R limits the production of pro-tumor macrophages, which, among other functions, is believed to aid in angiogenesis, tumor cell invasion and evasion of the immune system.

Following encouraging POC data from the Phase II study in biliary tract cancer (BTC), a pivotal open-label Phase IIb/III BTC trial (NCT03873532) in China has recently initiated, with the first patient dosed on 22 March; BTC represents a high unmet need due to limited treatment options and an increasing patient population. HCM is additionally developing the drug internationally: the global Phase Ib/II study (NCT02549937) in pancreatic NET (second-line in Sutent/Afinitor refractory cancer) and BTC started enrolling US patients in July 2018. These trials will be managed by HCM's clinical and regulatory team that is now in place in New Jersey, US.

With the growth and widespread use of PD-(L)1 inhibitor in the treatment of solid tumors, clinical trials combining these immune checkpoint inhibitors (ICIs) with CSF1(R) inhibitors have been initiated by several multinational pharmaceutical companies. HCM has recently initiated a Phase I dose escalation study (NCT03879057) in combination with Shanghai Junshi Biosciences' PD-1 inhibitor Tuoyi (toripalimab), which was recently approved in China for melanoma.

Exhibit 10: Surufatinib clinical development

Treatment	Indication	Sites	Trial	Notes
Surufatinib MT	Pancreatic NET	China	Phase III SANET-p	Interim analysis end-2019, if positive these could support an NDA submission early 2020
Surufatinib MT	Extra-pancreatic NET	China	Phase III SANET-ep	Met primary endpoint of PFS. China NDA submission expected by year end
Surufatinib MT	Biliary tract cancer (chemotherapy refractory)	China	Phase IIb/III NCT03873532	First patient dosed 22 March
Surufatinib MT	Pancreatic NET (second-line; Sutent/Afinitor refractory) Biliary tract cancer (chemotherapy refractory)	US	Phase Ib NCT02549937	US/EU registration study in planning
Surufatinib + Tuoyi (PD-1)	Solid tumors	China	Phase I NCT03879057	Trial enrolling patients
Surufatinib + Tuoyi (PD-1)	Solid tumors	US	Phase I	Safety run-in in planning
Surufatinib + HX008 (PD-1)	TBC	China	Phase I	Safety run-in in planning, will be managed partner by Taizhou Hanzhong

Source: Edison Investment Research, Hutchison China MediTech. Notes: NET – neuroendocrine tumors, MT – monotherapy.

Peak sales potential of $1.0bn across all indications

We forecast global peak sales for surufatinib of $953m across the NET and BTC indications. We have removed thyroid cancer and adjusted sales forecasts. Our peak sales forecasts for surufatinib in NET ($169m China, $454m RoW) are conservative as at this point. We have updated our assumptions for NET in China and now assume an incidence of 68,000 (vs 50,000 prevalence rate

previously) and 19 months of treatment (vs 12 months previously) in China. This is based on new data from Frost & Sullivan and Phase II median PFS data (19.4 months). However, we note a patient-access program similar to Elunate could reduce the number of months HCM receive reimbursement for surufatinib. Additionally, following the positive SANET-ep Phase III data we have upgraded our probability of success in NET to 90% from 75% previously. We forecast peak sales of $187m in BTC in China and $143m in RoW.

Global development of HMPL-523 and HMPL-689

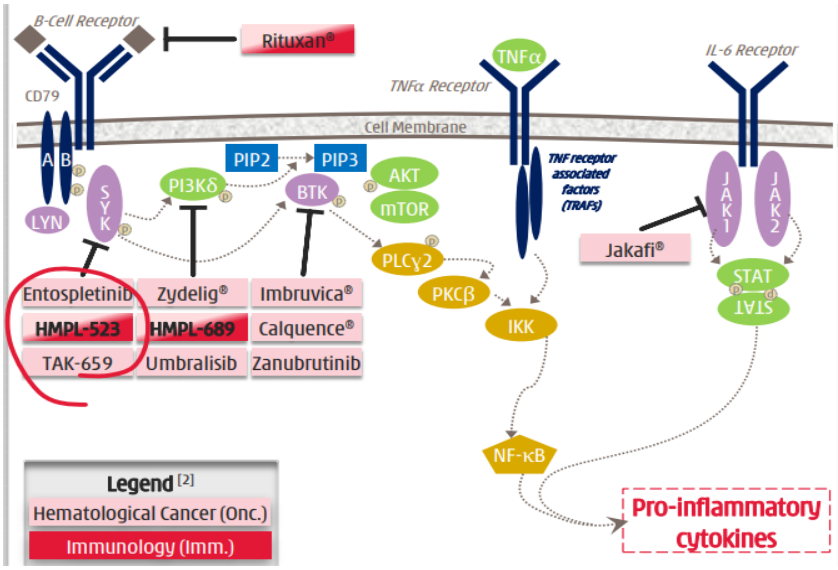
Longevity for R&D-driven biopharmaceutical companies is dependent on having a pipeline of innovative assets that span both indications and development phases. HCM's strategy to date has focused on developing best-in-class kinase inhibitors that target solid cancers; the next wave of internally developed assets, HMPL-523 (Syk inhibitor) and HMPL-689 (PI3Kδ inhibitor), are kinase inhibitors, which have a clinical focus for various hematological (blood) cancers and autoimmune conditions. Concurrent Global and Chinese clinical programs are ongoing, and recent IND approvals mean both assets have started US/EU Phase I clinical development for indolent NHL.

B-cell malignancies are a huge commercial opportunity

Hematological cancers arise in blood-forming tissue (leukemias and myelomas) or in the cells of the immune system (lymphomas), such as B cells or T cells. Treatment options vary according to cancer type and genetic burden. HMPL-523 and HMPL-689 are being developed for a range of B-cell malignancies (Exhibits 12 and 13). The commercial opportunity in treating hematological malignancies is substantial. Many novel treatments have reached blockbuster status in hematological cancer sales alone, for example, Revlimid ($8.9bn), Rituxan ($5.4bn) and Imbruvica ($4.5bn) in 2018. The US National Cancer institute SEER data estimate that in 2018 there were c 170 000 new cases of blood cancers, 33% of which were leukemias , 18% multiple myeloma (MM), 5% of Hodgkin's lymphoma (HL) and 44% with non-Hodgkin (NHL), which comprises over 30 types of aggressive (fast) and indolent (slow) B-cell and T-cell malignancies. Five-year survival rates (2008–2014) range from 27.4% in AML to 71.4% in NHL as patients relapse or become refractory (r/r) to current treatment options. Efficacy and safety data from the ongoing Phase I studies of both HMPL-523 and HMPL-689 will further define in which patient populations these assets could have utility, as well as give an early indication as to whether they could be used in combination with other treatments (safety data).

The B-cell signaling pathway is critical in hematological cancers. Approved novel drugs that target this pathway include Imbruvica, Zydelig, Jafaki and Rituxan (Exhibit 11). Targeting aberrant B cells is not only a proven strategy for the treatment of B cell-related malignancies, but also in autoimmune disorders such as multiple sclerosis (MS) and rheumatoid arthritis (RA), highlighted by the commercial success of antibodies such as Rituxan (rituximab) and Ocrevus (ocrelizumab). HCM is evaluating HMPL-523 in idiopathic thrombocytopenic purpura (ITP), an immune-mediated disease that results in low platelet levels.

Exhibit 11: B-cell receptor signaling



Source: Hutchinson China Meditech

Both HMPL-523 and HMPL-689 are small molecules designed to target kinases in the same B-cell receptor signaling axis as the Bruton's tyrosine kinase (BTK) inhibitor Imbruvica and Zydelig, which, like HMPL-689, acts through inhibition of PI3Kδ. Importantly, HCM retains the global development and commercialization rights to both of these assets and both could present significant growth drivers in the medium and long term. We believe a key factor in success will be whether both assets can demonstrate good safety profiles as monotherapy as this will indicate potential combination regimes, which is where we believe treatment paradigms are shifting in treating B-cell malignancies. Likewise, a well-tolerated treatment will be essential for these to show any utility in autoimmune disorders. To date, HMPL-523 has been dosed in c 110 patients and c 118 healthy volunteers, HMPL-689 in c 30 patients and c 48 healthy volunteers and both have shown no off-target toxicity.

HMPL-523: First-in-class opportunity for blood cancers

HMPL-523 targets Syk, an enzyme believed to be involved in diverse range of biological functions including in autoimmune disorders and hematological malignancies. In particular, Syk is involved in BCR signaling and is thought to promote the survival and maintenance of malignant cells. Syk sits just upstream of BTK and PI3Kδ and mediates their activation, therefore targeting it presents an alternative way of treating patients who are resistant or intolerant to Imbruvica or Zydelig (Exhibit 11). The clinical landscape for Syk inhibitors remains relatively competitive and in 2018 the US FDA approved the first Syk inhibitor, Rigel Pharmaceutical's fostamatinib (Tavalisse) for treating ITP. Entospletinib, developed by Gilead, is one of the most advanced clinical candidates for treating hematological malignancies.

HCM believes HMPL-523 is a potential best-in-class molecule and potentially first-in-class for hematological malignancies and we anticipate that launch in China in 2023 is feasible. Preliminary data presented at ASH2018 from the ongoing the Phase I/Ib study in China showed some promising signs of efficacy:

- 21 evaluable patients, with relapsed or refractory disease (median of three prior treatment lines, predominately chemotherapy and CD20 targeting antibodies);
- 19% showing partial response (3/10 follicular lymphoma [FL], 1/3 CLL/SLL); and
- 40% achieving stable disease (3/4 mantle cell lymphoma [MCL], 3/10 follicular lymphoma [FL], 1/3 CLL/SLL, 1/2 marginal zone lymphoma [MZL], 1/1 Waldenstrom macroglobulinemia [WM]).

Phase Ib dose expansion is ongoing in separate Chinese and Australian studies and will be used to guide a Chinese Phase II/III registrational study, which is planned to start in H219. In October 2018, a Phase I study was initiated, investigating the combination of HMPL-523 with azacitidine in treatment-naive Chinese patients with AML who are ineligible for standard chemotherapy. Following recent IND approval, an EU/US Phase I/II clinical study for HMPL-523 has started. In preclinical testing HMPL-523 has demonstrated a greater selectivity for Syk in comparison to fostamatinib (versus comparator kinases) and the first autoimmune indication HCM is planning for HMPL-589 is in Chinese patients with ITP.

In hematological malignancies, fostamatinib had shown early signs of efficacy in a Phase I/II study, particularly in r/r diffuse large B-cell lymphoma (DLBCL) patients (ORR 22%; 23 patients), but in a subsequent Phase II study efficacy was poor in a larger patient population (ORR 3%; 68 patients). Both Gilead and Takeda have Syk inhibitors, GS-9973 (entospletinib) and TAK-659, in clinical development for various B-cell related malignancies and have both shown promising signs of clinical efficacy as monotherapy regimes. Importantly, early efficacy data from a Phase II study for entospletinib begin to validate a Syk inhibitor as an alternative to Imbruvica or Zydelig: 61% ORR (41 patients; 95% CI 44.5–75.8%) in r/r CLL patients without prior exposure to a BTKi or PI3Kδi and 33% ORR (42 patients; 90% CI 21.7–45.3%) in those that had prior exposure.

Exhibit 12: HMPL-523 clinical development

Treatment	Indication	Sites	Trial	Notes
HMPL-523 MT	Multiple subtypes of relapsed or refractory B-cell malignancies	Australia	Phase I/Ib NCT02503033	Dose expansion now enrolling 40 pts with r/r CLL, SLL, MCL, FL and DLBCL
HMPL-523 MT	Indolent NHL	China	Phase I/Ib NCT02857998	Dose expansion now enrolling 152 pts with r/r CLL, SLL, MCL, FL and DLBCL patients
HMPL-523 MT	Indolent NHL	US/EU	Phase I/Ib NCT03779113	Trial enrolling patients
HMPL-523 + azacitidine (Vidaza)	first-line AML (elderly patients ineligible for standard chemotherapy)	China	Phase I/Ib NCT03483948	Trial enrolling patients
HMPL-523 MT	Idiopathic thrombocytopenic purpura (ITP)	China	Phase I	In planning

Source: Edison Investment Research, Hutchison China MediTech.

HMPL-689: Best-in-class potential for PI3Kδ

HMPL-689 is in a Phase I dose escalation study in Chinese patients with hematological malignancies and is expected to transition into dose expansion before the end of 2019, with top-line data expected in H120. The US FDA has approved three PI3Kδ inhibitors – Zydelig (idelalisib), Aliqopa (copanlisib) and Copiktra (duvelisib) – for the treatment of various blood cancers. Toxicity issues have been flagged with this class of drug, causing potentially fatal infections, diarrhea and liver toxicity (black box warnings); hence, safety data for HMPL-689 will be a critical marker for its potential to succeed as a best-in-class option for patients. Recent IND approval has enabled the start of a parallel US/EU Phase I/Ib study in patients with indolent NHL.

PI3Kδ is expressed predominately in haemopoietic (blood) cells where on activation by Syk, it works in conjunction with BTK to activate the AKT signaling; PI3Kδ signaling plays an important role in mediating the activation, development, survival and migration of malignant B cells. To date, the success of PI3Kδ inhibitors in treating B-cell malignancies, and their failings, has been defined by Gilead's Zydelig (idelalisib), which was the first PI3Kδ inhibitor approved by the US FDA (2014) as third-line treatment for SLL and FL and in combination with Rituxan for patients with relapsed CLL based on the following efficacy data:

- third-line follicular lymphoma (FL) – ORR 54% (95% CI, 42–66) out of 72 pts (six CR, 33 PR).
- third-line SLL – ORR 58% (95% CI, 37–77) out of 26 pts (15 PR).
- r/r CLL – mPFS for Zydleig + Rituxan NR (95% CI, 10.7 NR) vs Rituxan monotherapy 5.5 months (95%, 3.8–7.1) (HR 0.18, $p < 0.0001$).

Sales of Zydelig have stagnated (and declined slightly) since their peak in 2016 ($168m), due to the emergence of serious safety concerns, which forced Gilead to terminate six clinical trials.

HCM believes a variety of factors could position HMPL-689 as a best-in-class option versus Zydelig, Copiktra and Aliqopa; namely, its improved PI3K isoform selectivity profile, the reduced exposure levels required to have sufficient on-target effect and an improved drug-drug interaction profile, which should also enable the option to pursue safer combination regimens. The success that TG Therapeutics has seen in the development of its PI3Kδ inhibitor, umbralisib, demonstrates that a significantly improved tolerability profile can be achieved to enable safe combinations.

Exhibit 13: HMPL-689 clinical development

Treatment	Indication	Sites	Trial	Notes
HMPL-689 MT	Indolent NHL	China	Phase I/Ib NCT03128164	Dose escalation ongoing, dose-expansion expected to start before end-2019
HMPL-689 MT	Indolent NHL	US/EU	Phase I/Ib NCT03779113	Trial recruiting patients.

Source: Edison Investment Research, Hutchison China MediTech

Combinations are likely to be key in moving B-cell market

The next iteration of clinical development for both HMPL-523 and HMPL-689 will likely include combination regimes and the start of a Phase 1 trial investigating HMPL-523 with azacitidine as a first-line treatment is indicative of this. In the clinical landscape for Syk and PI3Kδ inhibitor development, safe and efficacious combination regimes are starting to emerge; in particular, we highlight TG therapeutics' Phase I/Ib trial data recently published in The Lancet, which showed the triplet combination of umbralisib (PI3Kδi), ublituximab (CD20) and Imbruvica (BTKi) achieved an impressive 84% ORR (37 of 44 patients) in patients with various advanced B-cell malignancies.

Conservative peak sales expectations

HMPL-523 and HMPL-689 are being evaluated for a broad range of hematological malignancies and HMP-523 has potential in less-common autoimmune disorders (such as ITP). These could add up to much larger commercial opportunities than our conservative peak sales for HMPL-523 ($143m in China, $584m RoW) and HMPL-689 ($102m in China, $468m RoW).

Other pipeline assets

HCM continues to invest in other assets including epitinib, theliatinib and early-stage discovery programs. Here we provide a brief update on these:

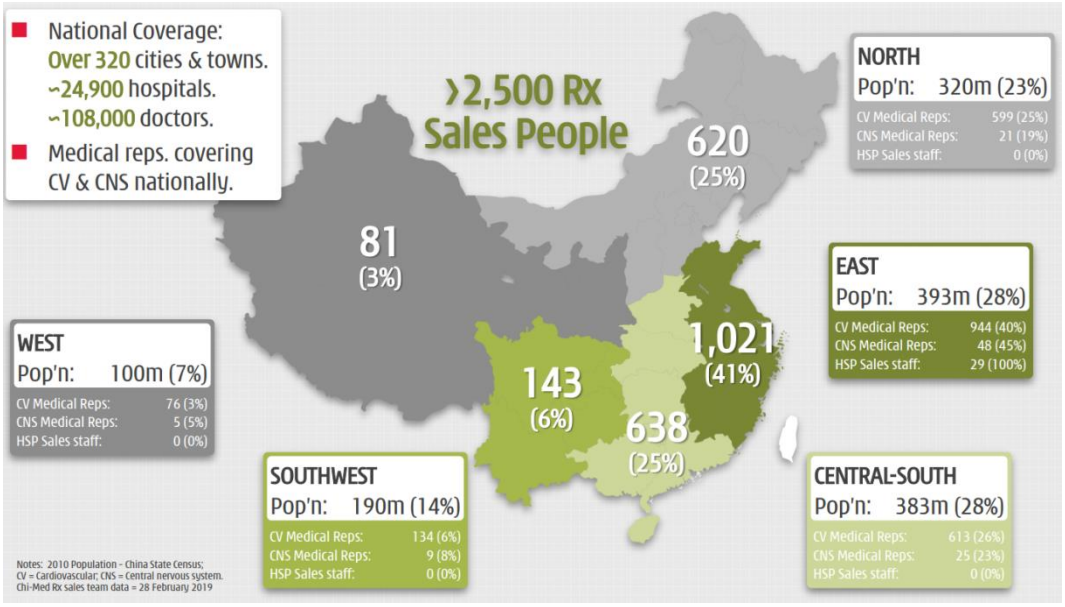
- Epitinib is being developed as monotherapy in glioblastoma (Phase Ib/II) and HCM is reviewing the commercial opportunity for EGFRm+NSCLC with brain metastasis in China. This follows changes in the competitive landscape with the inclusion of third-generation EGFR inhibitor Tagrisso on the Chinese NRDL and the availability of lower-priced generic versions of first-generation EGFR inhibitors Iressa and Tarceva.
- Theliatinib was in a Phase Ib study for esophageal cancer (China) but has been discontinued due to a short duration of response. We have removed this asset from our valuation until we have a clearer understanding of its development in solid tumors.
- HCM continues to invest in its discovery and preclinical pipeline. It is developing an early-stage portfolio of small molecules and antibodies for multiple targets (including validated and novel targets), with a focus on good tolerability and efficacy for combination strategies. In the long term HCM plans to move one novel drug candidate into global development per year.

CP highly cash generative

We expect HCM to capitalize on its knowledge of the Chinese market and drive sales through the utilization of its existing sales structure. A number of government-based reforms and other market forces (demographics, better access, higher investment) are changing the healthcare market in China. HCM has eight assets in clinical stage development, of which six are wholly owned and will be launched through the existing CP business. Manufacturing infrastructure and commercial teams will require further investment to meet demand and to grow the oncology organization to 200 by end 2020 (currently ~30). Over the past 18 years, HCM has built a broad manufacturing, marketing and distribution network that reaches across China, covering both consumer health (mainly OTC) and prescription-only drugs (including traditional Chinese medicine).

Full-year 2018 results published in March 2019 highlighted robust growth within the CP division. Total consolidated sales reported at $172.9m (-16%, FY17: $205.2m). Total sales of non-consolidated JVs increased by 13% to $491.5m on an adjusted non-GAAP basis (2017 excluded divested operations). Total consolidated net income attributable to HCM increased by 10% to $41.4m (adjusted non-GAAP basis excluding one-time gains of R&D subsidiaries and property compensation). The CP is subdivided into prescription drugs and consumer health. In Q119, revenues from CP were $46.4m driven by a 6.7% increase in prescription drugs (Q119 $37.8m, Q118 $35.5m) offsetting a 10% decline in consumer health (Q119 $8.5m, Q118 $9.4m). Exhibit 14 highlights the breadth of coverage in China.

Exhibit 14: CP in China



Source: Hutchison China MediTech

Bottom-line growth unaffected by two-invoice system

In 2018 HCM reported total CP sales (non-consolidated sales of subsidiaries and JVs from continuing operations) of $664.4m (+4%) contributing $41.4m (+10%) net attributable profit (NAP) to HCM equity holders. On a consolidated level, sales declined 16% to $172.9m and top-line declines were affected by the implementation of the China two-invoice system (TIS) and transitioning Seroquel (third-party product) sales from a gross sales revenue model to a service fee revenue model; total sales of non-consolidated JVs increased by 13% to $491.5m on an adjusted non-GAAP basis (2017 excluded divested operations). The CP is subdivided into prescription drugs and consumer health.

In 2018 non-GAAP HCM prescription drug sales declined by 1% to $408.5m (FY17: $411.0m) as a result of the TIS implementation and consolidated (non-GAAP) net income attributable to HCM grew 21% to $32.1m (FY17 $26.5m) excluding one-time gains. Prescription drugs represented 78% of HCM's CP net income in 2018 and consist of two pharmaceutical JVs:

- **Shanghai Hutchison Pharma (SHPL):** a 50/50 joint venture with Shanghai Pharmaceuticals (SHA: 601607) that focuses on prescription traditional Chinese medicines (TCMs). In 2018 SHPL restructured its distribution and logistics business due to the TIS regulations, which aim to reduce the number of layers in the drug distribution system in China. SHPL holds a large portfolio of registered drug licences, including its own and third party. In 2018, sales increased by 13% to $275.7m, which mainly was driven by price and volume growth of SHPL's main product, the She Xiang Bao Xin Wan (SXBX) pill for coronary heart disease ($233.1m, +11%). SXBX now has 17% market share for China's botanical prescriptions market in coronary heart disease.
- **Hutchison Sinopharm**: a third-party prescription logistics and distribution service that reported sales of $132.8m in 2018 (-20%). Hutchison Sinopharm is the exclusive marketing agent for AZN's Seroquel, which holds a 6% market share in China's c $0.9bn atypical anti-psychotic drug market. Reported 2018 sales were affected by the new China TIS that came into effect in October 2017. Hutchison Sinopharm can no longer book gross sales of Seroquel in its top-line revenues and has shifted to a fee-for-service model; there is no impact on a profitability basis and service fees paid to Hutchison Sinopharm increased 51% to $17.2m in 2018. Hutchison Sinopharm is being affected by the 4+7 Quality Consistency Evaluation (QCE) bidding process that led to a trimming of the 2019 product portfolio as not all HCM's third-party generic partners won the 4+7 QCE bids. This may affect consolidated sales slightly; there is little impact on net profitability given the very low-margin business.

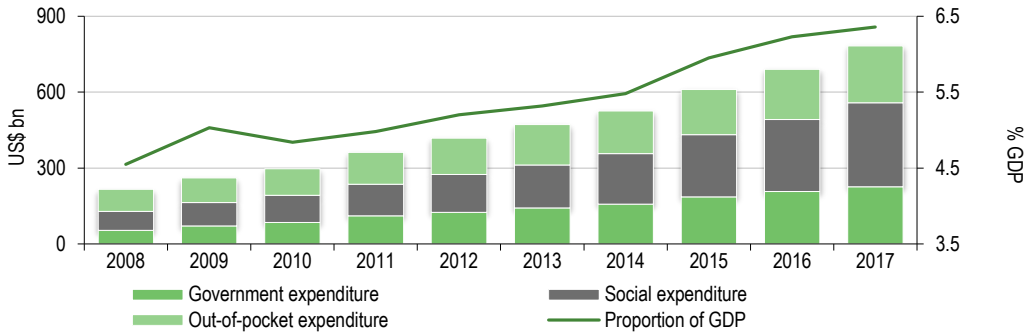
Consumer health consists of two main subsidiaries (consolidated) and a JV with Hutchison Baiyunshan (HBYS, non-consolidated). In FY18 consolidated sales were up slightly (by 3%) to $40.1m, non-consolidated joint venture sales declined 5% to $215.8m; total consolidated net income attributable to HCM decreased 16% to $9.3m, highlighting that consumer health represents 22% of CP net income.

- **Hutchison Baiyunshan (HBYS**): a 50/50 joint venture with Guangzhou Baiyunshan (SHE: 000522), principally focused on OTC TCM with 189 registered TCM products. Sales of HBYS's two main products were flat y-o-y ($118.9m), with a decline (-4%) in Fu Fang Dan Shen tablets for angina (FY18: $56.3m) offset by Banlangen granules (anti-viral cold/flu), sales of which grew by 4% to $62.6m.

Second-largest and fastest-growing healthcare market

The Chinese healthcare market has demonstrably benefited from governmental social and strategic commitments, a burgeoning middle class and growth in wealth (polarized between rural and urban and more wealthy provinces) that gives people the ability and willingness to pay for goods where the direct consumer benefit can be seen. Since 2015, China has been estimated to be the second-largest healthcare market in the world, with the US ranked first. In 2017, China's expenditure on healthcare was still a relatively small percentage of its output, at 6.4% of GDP ($783bn of $12.3tn), in comparison to the US, which spends 17.9% of GDP on healthcare ($3.5tn of $19.5tn).

Exhibit 15: China's annual healthcare expenditure



Source: National Bureau of Statistics of China

Robust growth in the Chinese market has been underpinned by a series of healthcare reforms implemented by the PRC government that have looked to improve access on several levels and aim to provide every Chinese resident (rural and urban) with basic healthcare coverage by 2020. In October 2016 the government passed its 15-year blueprint 'Healthy China 2030', which aims to grow the expenditure in the healthcare industry in China to $2.4tn and achieve health standards on par with developed countries. Similar to the multifactorial support of past plans, regulatory reforms focus on expanding China's universal health coverage and developing a world-class life sciences industry backed by intellectual property support. Below we have highlighted some shifts in regulation that have had, or will have, an impact on HCM's commercial operations in China:

- **Insurance coverage**: government measures have centered on expanding medical cover to 95% of the population. However, the depth of coverage varies across the three publicly funded insurance funds and the various provinces due to differing wealth levels. The China National Bureau of Statistics suggests 56% of the population had medical insurance in 2018 vs 17% in 2007. The shift of focus is now to improve the quality of coverage and diversify insurance cover to increase access to more costly therapies.
- **NRDL**: revisions to drug inclusions (and exclusions) on China's NRDL have become more frequent in the last few years and since 2017, 128 Western drugs have been placed on the NRDL, including 32 for oncology. Inclusion is subject to pricing negations (discounting) as the scope of the NRDL is to improve patient access to domestic and international developed drugs.
- **TIS:** the regulatory reform implemented in 2017 and fully adopted in 2018 has resulted in a new invoicing system that reduces the layers in the pharmaceutical value chain, requiring a drug manufacturer to issue only one invoice to a distributor, followed by the distributor issuing a second invoice directly to the end hospital, with the aim of consolidating drug distribution and reducing drug prices.
- **4+7 QCE:** a pilot program implemented in November 2018, centralizing the tendering process for drugs included in the National Medicines Catalogue for public medical institutions across 11 major cities, around one-third of the market. The aim of the 4+7 system is to consolidate a fragmented generic drug market and drive down prices. HCM believes this is likely to lead to Hutchinson Sinopharm's portfolio contracting and a decline in sales in the near term but as cost savings are realized by the state, in the long term there will be more scope to include more innovative medicines on reimbursement lists.

Oncology market in China is beginning to blossom

With China contributing a significant portion to cancer incidence and mortality globally, c 24% of new cases (4.3m of 18.1m) and c 30% of deaths in 2018 (source: The Global Cancer Observatory), the market opportunity for targeted oncology drugs in China is huge and, until recent years, largely

untapped; despite their proven efficacy, the high cost of targeted therapies has historically proven to be a major limitation of growth. Pricing strategies and inclusion to the NRDL is of great importance to successfully commercializing oncology drugs in China. With 15 oncology drugs included in the NRDL in July 2017 and 17 more in October 2018, there are strong signs that the oncology market in China is starting to blossom, underlined by strong growth. Since the inclusion of Herceptin and Avastin into the NRDL in 2017, Roche has experienced a c four-fold increase in penetration:

- Herceptin: 66% discount led to a 383% increase in volume and 31% sales growth in 2018.
- Avastin: 62% discount led to a 452% increase in volume and 72% sales growth in 2018.

Valuation

Our SOTP valuation of HCM has reduced (Exhibit 16) to $5.6bn or $42.23/ADS (vs $6.5bn in September 2018).

We value the innovation platform (IP) at $4,004m and placing CP's 2019e share of net profit on a 20.4x rating gives a valuation of $800.4m ($6.00/ADS). Adding in April 2019 net cash, terminal value and netting off unallocated costs results in a value of $5.6bn or $42.23/ADS. We use a 10% discount rate and 1% growth rate in calculating the terminal value of $1,022m, which represents 20% of our total valuation of the company. We note the significant increase in our terminal value is driven by the adjustment of time horizons, notably the terminal value now captures a greater proportion of key product sales. Additionally, the separation of some centralized costs from our product models (unallocated costs of $430m or $3.25/ADS) has positively affected the terminal value ($3.70/ADS to $7.67/ADS). Our standard discount rate assumption is 10% for companies with approved products and minimal development risk.

For the innovation platform we have adjusted our valuation to reflect the success of the SANET-ep Phase III trial, the failure of fruquintinib monotherapy in third-line NSCLC (FALUCA), the cessation of enrolment in the SAVOIR (savolitinib monotherapy in PRCC) study and the discontinuation of the clear cell RCC monotherapy trial (component of CALYPSO trial) in favor of combination strategies. Launch dates for key assets have been pushed back materially as we gain more clarity on global development timelines particularly in relation to combination strategies; this has had the most significant negative impact on our valuation. On the other hand, we have brought our time to peak sales in China in line with our assumptions for ROW as market dynamics in China continue to positively shift towards quicker uptake of innovative therapies. Finally, we have altered peak sales assumptions taking into account revised clinical trial data, changes in oncology treatment paradigms and pricing strategies.

With the CP, we look at the earnings multiples of peers quoted on the Chinese stock exchanges. Using a 20.4x multiple (in line with the sector (non-weighted) average for comparable domestic Chinese companies) on the 2019 forecast net attributable profit of $39.2m for the CP unit results in a valuation of $800.4m.

Exhibit 16 details the breakdown of contribution from products by indication to our risk-adjusted NPV. Projects in preclinical development are not yet included in our valuation and we have removed valuation of assets where we are uncertain on timeline or strategy for development. We have revised our R&D and S&M costs per asset and introduce an unallocated cost line to account for the increasing requirement to invest across the business globally in centralized costs (expansion of US and international operations).

We note that under US GAAP, jointly controlled entities are not consolidated proportionately as these assets are now effectively off the balance sheet. This means the cash held by the jointly controlled entities is not included in our valuation of the group.

Exhibit 16: HCM SOTP valuation

Product	Indication	Launch/Peak	Peak sales ($m)	Value ($m)	Probability (%)	rNPV ($m)	rNPV/ADS ($/ADS)
savolitinib (AZD6094/volitinib)	PRCC	2024/2029 (China)	$64m (China)	99.9	50%	61.4	0.46
		2022/2026 (RoW)	$267m (RoW)	71.1	75%	50.1	0.38
	ccRCC	2025/2029 (China)	$169m (China)	90.0	35%	27.0	0.20
		2023/2028 (RoW)	$664m (RoW)	95.8	35%	33.5	0.25
	NSCLC	2022/2030 (China)	$387m (China)	252.8	75%	187.9	1.41
		2022/2029 (RoW)	$1.7bn (RoW)	361.8	75%	271.4	2.04
	Gastric cancer	2023/2030 (China)	$326m (China)	140.3	35%	45.0	0.34
		2024/2028 (RoW)	$757m (RoW)	130.7	35%	45.7	0.34
fruquintinib	CRC	2018/2024 (China)	$211m (China)	96.4	100%	96.4	0.72
		2023/2028 (RoW)	$565m (RoW)	1,169.7	75%	874.0	6.56
	NSCLC	2025/2031 (China)	$393m (China)	79.8	50%	32.3	0.24
		2025/2030 (RoW)	$721m (RoW)	784.7	50%	371.4	2.79
	Gastric cancer	2021/2028 (China)	$276m (China)	163.8	75%	120.9	0.91
		2025/2030 (RoW)	$392m (RoW)	471.0	50%	223.9	1.68
Surufatinib	NET	2021/2028 (China)	$169m (China)	398.7	90%	358.1	2.69
		2024/2029 (RoW)	$454m (RoW)	636.5	50%	301.4	2.26
	BTC	2022/2028 (China)	$194m (China)	393.0	75%	293.0	2.20
		2024/2029 (RoW)	$148m (RoW)	176.8	50%	82.7	0.62
Epitinib	Glioblastoma	2023/2028 (China)	$43m (China)	133.7	30%	36.5	0.27
HMPL 523	Hematological cancers	2023/2029 (China)	$149m (China)	280.0	30%	78.3	0.59
		2025/2029 (RoW)	$584m (RoW)	776.3	30%	220.5	1.65
HMPL-689	Hematological cancers	2024/2030 (China)	$108m (China)	151.5	30%	36.9	0.28
		2025/2030 (RoW)	$486m (RoW)	571.8	30%	155.6	1.17
Commercial Platform				800.4	100%	800.4	6.00
Unallocated costs				(433.2)	100%	(433.2)	(3.25)
Net Cash April 2019				236.2	100%	236.2	1.77
Terminal Value				1,022.4	100%	1,022.4	7.67
Valuation				$9,151.9		$5,629.7	$42.23
Valuation of IP only				$6,026.4		$4,003.8	$30.03

Source: Edison Investment Research. Note: Non-risk adjusted NPV per ADS assumes 100% probability of success. Number of ADS outstanding 133.3m.

Financials

HCM reported consolidated group revenues of $214.1m in FY18 (-11.1%, FY17 $241.2m) and net loss of $74.8m (FY17 $26.7m). CP reported consolidated sales of $172.9m, a decline of 16% (FY17 $205.2m) following the new policy implemented by the China government during 2018 (TIS and 4+7 QCE bidding process). The TIS impact means that consolidated JV Hutchison Sinopharm now reports service fees versus prior revenue recognition of gross sales from third parties; overall profit contribution from these business activities substantially remains unchanged. Total consolidated net income from CP actually increased 10% to $41.4m (FY17 $37.5m) on an adjusted (non-GAAP basis). We forecast consolidated CP revenues of $154.2m in 2019 and $157.6m in 2020.

IP reported consolidated revenues of $41.2m (reflecting in the main service fees from partners, a $13.5m milestone payment on Elunate China approval and $0.3m royalty income from Lilly). In FY18 IP reported a net loss of $102.4m (FY17 $51.9m). We forecast IP revenues of $28.7m in 2019 and $36.8m in 2020, largely driven by developmental royalties on sales on Elunate and service fees from partners.

Profit before tax at the group level reported a loss of $86.6m in FY18 (versus a loss of $53.5m in FY17). R&D expenses increased significantly to $114.2m in FY18, reflecting investment throughout the portfolio and expansion of the US and international clinical and regulatory operations. S&M expenses decreased to $17.7m in FY18 (versus $19.3m in FY17) and administrative expenses

increased to $30.9m (versus $24.0m in FY17). For FY19 HCM has narrowed guidance to R&D expenses in the range of $160–200m and adjusted non-GAAP group net cash flow excluding financing activities of $120–150m.

We expect R&D expenses to increase to $175.5m in 2019 and $184.0m in 2020 (reported GAAP basis), reflecting the substantial need for investment in the burgeoning clinical trial programs across the IP division, including the increased investment in China and global trials plus the initiation of combination strategies across the portfolio.

We forecast net losses at the group level of $142.9m in 2019 and $145.2m in 2020. HCM reported a healthy cash position with available cash resources of $391.2m (at 31 March 2019) at the group level (cash and cash equivalents and short-term investments of $271.9m, and unutilized bank borrowing facilities of $119.3m). In May 2019 HCM entered into a credit agreement with HSBC for an additional $51.3m unsecured credit facility. Additionally, HCM's non-consolidated joint ventures (SHPL, HBYS and NSP) held $59.2m (at 31 December). HCM reported debt of $26.8m at 31 April 2019. This implies a net cash position of $236.2m. In terms of cash utilization by operations, we forecast $124.3m in 2019 and $127.2m in 2020.

HCM has published Q119 numbers, headline figures are shown in Exhibit 17.

Exhibit 17: Headline Q119 P&L figures

$m	Q118	Q119
Total revenues	52.3	52.2
CP sales	44.9	46.4
IP sales	7.4	5.8
Cost of sales	37.1	41.0
R&D	28.7	33.3
SG&A	11.6	14.0
Net profit	(10.4)	(19.1)

Source: HCM accounts, Edison Investment Research

Exhibit 18: Financial summary

US$'000s	2016	2017	2018	2019e	2020e
December	US GAAP	US GAAP	US GAAP	US GAAP	US GAAP
PROFIT & LOSS					
Revenue	216,080	241,203	214,109	182,885	194,426
Cost of Sales	(156,328)	(175,820)	(143,944)	(128,232)	(129,499)
Gross Profit	59,752	65,383	70,165	54,653	64,928
Research and development	(66,871)	(75,523)	(114,161)	(175,500)	(184,000)
Other overheads	(39,578)	(43,277)	(48,645)	(51,604)	(52,752)
EBITDA	(44,264)	(50,692)	(88,975)	(167,811)	(166,358)
Operating Profit (before amort. and except.)	(46,697)	(53,417)	(92,641)	(172,452)	(171,824)
Intangible Amortization	0	0	0	0	0
Operating Profit	(46,697)	(53,417)	(92,641)	(172,452)	(171,824)
Net Interest	(1,129)	(235)	4,969	1,988	(739)
Exceptionals	0	0	0	0	0
Profit Before Tax (norm)	(47,356)	(53,536)	(86,655)	(170,464)	(172,562)
Profit Before Tax (reported)	(47,356)	(53,536)	(86,655)	(170,464)	(172,562)
Tax	(4,331)	(3,080)	(3,964)	(5,004)	(5,200)
Equity investments, after tax	66,244	33,653	19,333	39,233	40,813
Profit After Tax (norm)	14,557	(22,963)	(71,286)	(136,234)	(136,949)
Profit After Tax (reported)	14,557	(22,963)	(71,286)	(136,234)	(136,949)
Minority	(2,859)	(3,774)	(3,519)	(5,000)	(5,000)
Discontinued operations	0	0	0	0	0
Net profit (norm)	11,698	(26,737)	(74,805)	(141,234)	(141,949)
Net profit (reported)	11,698	(26,737)	(74,805)	(141,234)	(141,949)
Average Number of Shares Outstanding (m)	597.2	617.2	664.3	666.6	666.6
EPS - normalized (c)	2.0	(4.3)	(11.3)	(21.2)	(21.3)
EPS - normalized and fully diluted (c)	19.6	(4.3)	(11.3)	(21.2)	(21.3)
EPS - (reported) (c)	2.0	(4.3)	(11.3)	(21.2)	(21.3)
Average number of ADS outstanding (m)	119.4	123.4	132.9	133.3	133.3
Earnings per ADS - normalized ($)	0.01	(0.02)	(0.06)	(0.11)	(0.11)
Earnings per ADS ($)	0.01	(0.02)	(0.06)	(0.11)	(0.11)
BALANCE SHEET					
Fixed Assets	175,057	165,737	161,577	176,169	192,947
Intangible Assets	3,606	3,738	3,533	3,301	3,028
Tangible Assets	9,954	14,220	16,616	22,207	27,014
Investments	161,497	147,779	141,428	150,661	162,905
Current Assets	167,380	432,195	370,541	233,688	71,281
Stocks	12,822	11,789	12,309	10,540	10,644
Debtors	49,349	53,566	56,392	56,000	29,830
Cash	79,431	85,265	86,036	41,259	29,919
St investments	24,270	273,031	214,915	125,000	0
Other	1,508	8,544	889	889	889
Current Liabilities	(95,119)	(104,600)	(85,479)	(101,457)	(94,778)
Creditors	(35,812)	(25,344)	(26,180)	(42,158)	(35,479)
Short term borrowings	(19,957)	(29,987)	0	0	0
Other	(39,350)	(49,269)	(59,299)	(59,299)	(59,299)
Long Term Liabilities	(43,258)	(8,366)	(34,384)	(34,384)	(34,384)
Long term borrowings	(26,830)	0	(26,739)	(26,739)	(26,739)
Other long-term liabilities	(16,428)	(8,366)	(7,645)	(7,645)	(7,645)
Net Assets	204,060	484,966	412,255	274,016	135,066
Minority	(19,790)	(23,233)	(23,259)	(28,259)	(33,259)
Shareholder equity	184,270	461,733	388,996	245,757	101,807
CASH FLOW					
Operating Cash Flow	(9,569)	(8,943)	(32,847)	(122,687)	(124,341)
Net Interest	0	0	0	0	0
Tax	0	0	0	0	0
Capex	(4,327)	(5,019)	(6,364)	(10,000)	(10,000)
Acquisitions/disposals	0	0	0	0	0
Dividends	(564)	(1,594)	(1,282)	(2,000)	(2,000)
Equity financing and capital movements	97,076	291,737	(2,322)	0	0
Other	(29,270)	(255,761)	50,116	89,910	125,000
Net Cash Flow	53,346	20,420	7,301	(44,777)	(11,341)
Opening net debt/(cash and ST investments)	18,051	(56,914)	(328,309)	(274,212)	(139,520)
Increase/(decrease) in ST investments	24,270	248,761	(58,116)	(89,915)	(125,000)
Other	(2,651)	2,214	(3,282)	0	0
Closing net debt/(cash and ST investments)	(56,914)	(328,309)	(274,212)	(139,520)	(3,180)

Source: HCM accounts, Edison Investment Research

Contact details	Revenue by geography
48th Floor, Cheung Kong Center, 2 Queen's Road Central, Hong Kong +852 2128 1188 www.chi-med.com	N/A

Management team

Chairman: Simon To	CEO: Christian Hogg
Simon To is managing director and founder of Hutchison Whampoa (China), with over 30 years' service, having built the business from a small trading company to a large investment group with interests in aviation, hotels, port logistics, consumer products, residential developments, power plants and transport infrastructure. He is chair or director of a number of China-focused businesses and joint ventures. He has a BSc in mechanical engineering from Imperial College, London, and an MBA from Stanford.	Christian Hogg joined the company in 2000 and has, as CEO, led all aspects of the creation, implementation and management of Hutchison China MediTech's strategy, operations in both the IP and CP, and London and New York IPOs. This included establishing research collaborations with AZN and Lilly and operating joint ventures with Nestlé, Hain Celestial, Shanghai Pharmaceuticals, Guangzhou Pharmaceuticals and Sinopharm. Previously, he spent 10 years with Procter & Gamble, including managing the detergent business in China and the global bleach business. He has a BSc in civil engineering from Edinburgh and an MBA from Tennessee.
CFO: Johnny Cheng	**CSO: Weiguo Su**
Johnny Cheng has been CFO since 2008. Previously, he was VP finance of Bristol Myers Squibb in China and a director of Sino-American Shanghai Squibb Pharmaceuticals and BMS (China) Investment Co. He also spent eight years in various financial positions with Nestlé China and was an auditor with Price Waterhouse (Australia) and KPMG (Beijing). He has a bachelor of economics from the University of Adelaide and is a member of the Institute of Chartered Accountants in Australia	Weiguo Su is chief scientific officer, with 11 years' experience at the company. He created HCM's R&D strategy IP and led all pipeline discovery. Previous experience includes director of medicinal chemistry at Pfizer. He spent seven years at Harvard under E J Corey, the Nobel Prize winning medicinal chemist. Weiguo was one of the first mainland Chinese to be granted a scholarship to study at Harvard.

Principal shareholders	(%)
CK Hutchison Holdings Limited (through its wholly owned subsidiary Hutchison Healthcare Holdings Limited)	51.15
Prudential Group	5.10
Mitsui & Co	3.80

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Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1,185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia